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Review Article

Comprehensive management of pneumonia in older patients

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ABSTRACT

Pneumonia is a leading cause of death and functional decline in the older population. Diagnosis of pneumonia conventionally includes the presence of respiratory signs and symptoms, systemic signs of infection and a radiographic demonstration of lung involvement. Pneumonia diagnosis in the very old patient is compromised by atypical and unspecific presentation, resulting in a high proportion of false positive diagnosis. Chest radiograph is frequently of low quality and inconclusive in older patients. Computed tomography scan and chest ultrasound may provide valuable diagnostic confirmation in uncertain cases. Bacterial pneumonia has been mainly studied, but viruses, among which influenza, SARS-CoV-2, and respiratory syncytial virus, are increasingly recognized as major players. The decision to treat pneumonia is usually based on a triple assessment of diagnostic probability, disease severity and the general assessment of the patient (frailty, comorbidities, place of living, and goals of care). Antimicrobial treatment is probabilistic, targeting common pathogens. The optimal antibiotic treatment depends on epidemiological data, setting of acquisition, comorbidities, risk factors for methicillin-resistant *Staphylococcus aureus, Pseudomonas aeruginosa*, or aspiration pneumonia, and severity. Recent controlled trials have demonstrated the non-inferiority of short regimen in non-severe community acquired pneumonia, even in older individuals and a five-day antibiotic treatment is recommended in case of clinical improvement. Pneumonia management in older patients requires a comprehensive approach, including control of comorbidities (particularly cardiovascular), nutritional support, rehabilitation, and prevention of aspiration. Finally, pneumonia may be a pre-terminal event in many patients, requiring advanced-care planning and prompt instauration of palliative management.

1. Introduction

Pneumonia is a bacterial, viral, fungal, or parasitic infection of lung parenchyma, resulting in significant local and systemic inflammation. Pneumonia is the leading infectious cause of hospitalization and death worldwide. In high-income countries, older individuals are particularly affected [1]. Pneumonia is classified as community acquired (CAP), nursing home acquired (NHAP), hospital acquired (HAP), or associated with mechanical ventilation (VAP) (Fig. 1) [2]. Aspiration pneumonia (AsP) is a distinct form of pneumonia that develops in patients with dysphagia, or when macro aspiration of oropharyngeal content is obvious. AsP is an infection caused by specific microorganisms and the main form of pneumonia in older frail patients, whereas chemical pneumonitis is an inflammation due to the acidity of gastric contents. [3] Pneumonia in the immunocompromised host has many specific aspects and is outside of the scope of this review.

Though antibiotics are highly effective in killing most usual bacterial pathogens, the mortality remains far higher than in urinary or digestive tract bacterial infections. This can in part be attributed to pneumonia being a frequent terminal event in the very old (the widely quoted "old

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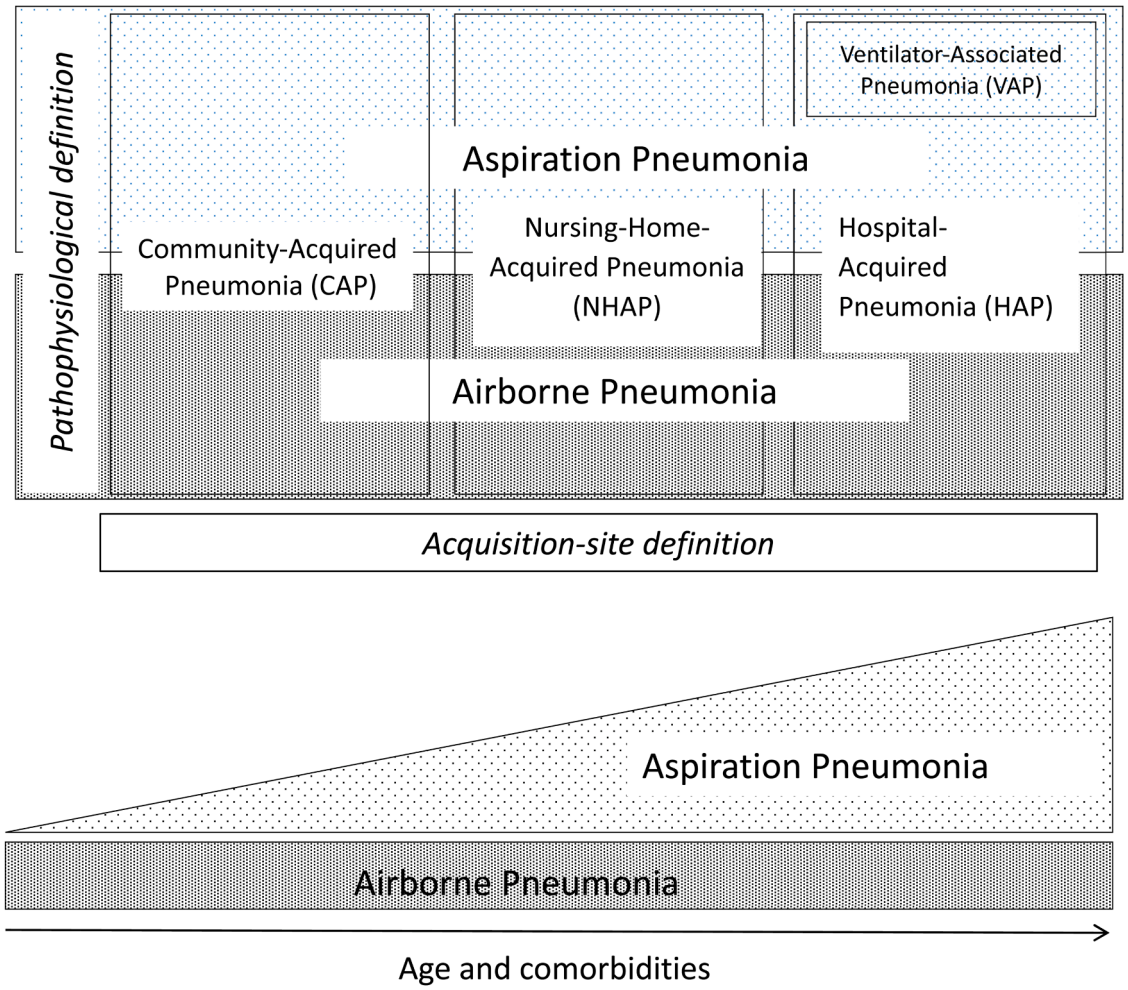

Fig. 1. Pathophysiological and acquisition-site classifications of pneumonia.

man's friend") [1,4]. In 2019, respiratory infections caused an estimation of 2.18 million deaths worldwide, half of them in adults over 70 [1]. Mortality rises steeply with age, from 5 % in <65, to 14 % in >80; further increasing to 20 % and 43 % respectively in the presence of comorbidities [5]. Long-term mortality is also increased, 1 in 3 adults dying the year following an hospitalisation for CAP [6]. Mortality in patients with AsP is twice as high as in patients with non-aspiration CAP, maybe due to a higher prevalence of severe comorbidities [3,7].

The higher incidence of CAP and higher mortality in older age are explained by age-related changes affecting the respiratory tract and the immune system. Accumulating comorbidities and ceiling decisions in the level of care (e.g. not providing full life support in shock or respiratory failure) are other contributors.

2. Pathogens

Many microorganisms can cause pneumonia, though bacterial pneumonia has been mostly studied. However, viruses are increasingly recognized as a major player, as recently highlighted by the Covid-19 pandemic.

Main microbiological aetiologies are presented in table 1. *Streptococcus pneumoniae* is the most common bacteria isolated from older patients. However, its incidence is declining in Western countries, probably secondary to pneumococcal vaccines and decrease in smoking prevalence. In contrast, there is an increase in the relative incidence of *Haemophilus influenzae* [8,9] and *Moraxella catharralis. Staphylococcus aureus* and *Enterobacteriaceae* are frequent in older patients, likely because of the frequency of AsP [3]. While nursing-home patients frequently present with Gram-negative pneumonia, these infections are rare (around 3 %) in home-dwelling patients aged over 80 year [10]. *Mycoplasma pneumoniae* were less frequently found than in younger patients until the recent epidemic [8,9,11]. Legionellosis is frequent in very old patients [12], and should be systematically considered in severe pneumonia or evocative clinical context (acquisition in summer or fall, hyponatremia, fever> =39.5 C) [13]. Identification of *Legionella spp* has significant consequences for treatment, as it is naturally resistant to beta lactams. Antibiotic-resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*, should be considered in case of antimicrobial failure, especially in patients dwelling with chronic respiratory disease, in intensive care settings. Community-acquired MRSA represents an uncommon cause of pneumonia in older adults [14]. Multidrug resistant *P. aeruginosa* should be considered among older with non-cystic fibrosis bronchiectasis, particularly among women [15]. Factors predisposing patients to infection with Gram-negative multi-drug resistant pathogens are prior colonization with a resistant bacteria, recent hospitalization, and treatment with parenteral antibiotics within the last 90 days [16]. Probabilistic regimen should be adapted to local epidemiology when these factors are present. According to recent data, anaerobes are no more frequent in AsP than in other forms of pneumonia [17]. *Mycobacterium* tuberculosis is the most common etiology, followed by *S. pneumoniae*, in low-middle income countries [18]. Secondary to the dissemination of molecular diagnostic techniques, influenza, SARS-CoV-2 and respiratory syncytial virus (RSV) have been identified as frequent causes of pneumonia during epidemics,

Table 1
Main pathogens involved in pneumonia according to pathophysiology and place of acquisition.

Aspiration Pneumonia		Airborne Pneumonia	
Community acquired pneumonia Nursing-home acquired pneumonia	- *Enterobacteriaceae* - Methicillin-sensitive *Staphylococcus aureus* - *Anaerobes*	Interhuman transmission	- *Streptococcus pneumoniae* - *Haemophilus influenzae* - *Moraxella catarrhalis* - *Chlamydophila* spp. - *Mycoplasma pneumoniae* - Respiratory viruses (influenza virus, SARS-CoV-2, respiratory syncytial virus, parainfluenza virus, human metapneumovirus, rhinoviruses, common human coronaviruses) - *Mycobacterium* spp. - *Pneumocystis jirovecii*
Hospital acquired pneumonia Ventilator-associated pneumonia	- *Enterobacteriaceae* - Methicillin-sensitive or resistant *Staphylococcus aureus* - *Pseudomonas aeruginosa* - *Stenotrophomonas* spp. and *Acinetobacter* spp. - *Anaerobes* - Viruses (SARS-CoV-2, influenza, RSV)	Environmental transmission	- *Aspergillus spp,* - *Legionella spp*

with older adults being an important target for RSV [19]. They are preventable with vaccination, and specific treatment may be administered for influenza (oseltamivir, baloxavir) and SARS-CoV-2 (remdesivir, nirmatrelvir/ritonavir). Molecular test performance also has identified *Pneumocystis jirovecii* as a cause of pneumonia among patients with acute respiratory failure [20], perhaps associated with immunosenescence.

3. Diagnosis

3.1. Clinical signs and symptoms

Diagnostic uncertainty prevails in the majority of cases of suspected pneumonia, especially in older patients. This translates in half the patients hospitalized for pneumonia having discordant diagnoses from initial presentation to discharge [21]. As for younger patients, the most common symptoms are acute cough, dyspnoea, chest pain and sputum. However, the triad of cough, fever and dyspnoea is absent in half the patients with pneumonia [22]. In older patients, pneumonia may present with acute development of geriatric syndromes (fall, delirium, decline of general condition, new incontinence) without classic respiratory or infectious manifestations. The poor specificity may lead to two common pitfalls in this age group: delayed diagnosis and over-diagnosis. Atypical presentation is a marker of poor prognosis [23,24].

3.2. Lung imaging

Radiologic imaging is needed to confirm parenchymal invasion, and allows localisation of lung injury, extent of disease, and complications. Chest X-ray (CXR) is the main imaging modality used. However, it may be impossible to obtain high quality CXR (bedridden patients, lack of cooperation in delirium) and identification of lung infiltrate can be jeopardized by heart failure, deformation of the rib cage, emphysema, or sequalae (Fig. 2). Consequently, inter-observer agreement on the interpretation of CXR for the diagnosis of pneumonia is poor [25]. Compared with chest CT, sensitivity of CXR is 43–65 % and specificity 93 % [26,27].

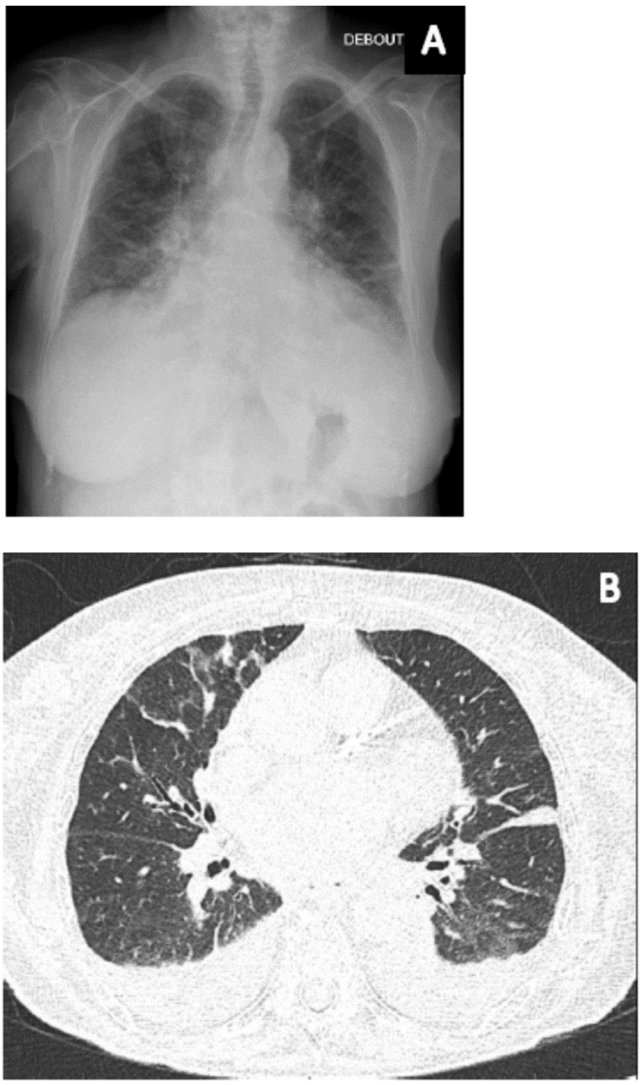

Fig. 2. Chest X-ray (A) and CT scan (B) in an 85-year-old patient presenting with a febrile cough. While the X-ray was compatible with the initial diagnosis of bacterial pneumonia, the CT scan corrected the diagnosis to that of left heart failure. Blood and urine cultures confirmed the extra-pulmonary origin of the fever (pyelonephritis with bacteraemia).

Chest CT can be done with a low radiation dose and without injection of iodinated contrast. It has a higher diagnostic yield. In a prospective study of patients over 65, it was particularly useful for ruling out pneumonia (Fig. 2). The impact was greatest in patients with intermediate pre-test probability (Fig. 3) [28]. However, availability of CT-scan may be limited, and associated costs are a concern for such a frequently suspected disease.

Lung ultrasound (LUS) is an attractive alternative increasingly used. It is a quick, non-irradiating, imaging modality that can be used at the patient's bedside, in the outpatient practice or in the emergency department by non-radiologists (point-of-care, POCT, if available). LUS

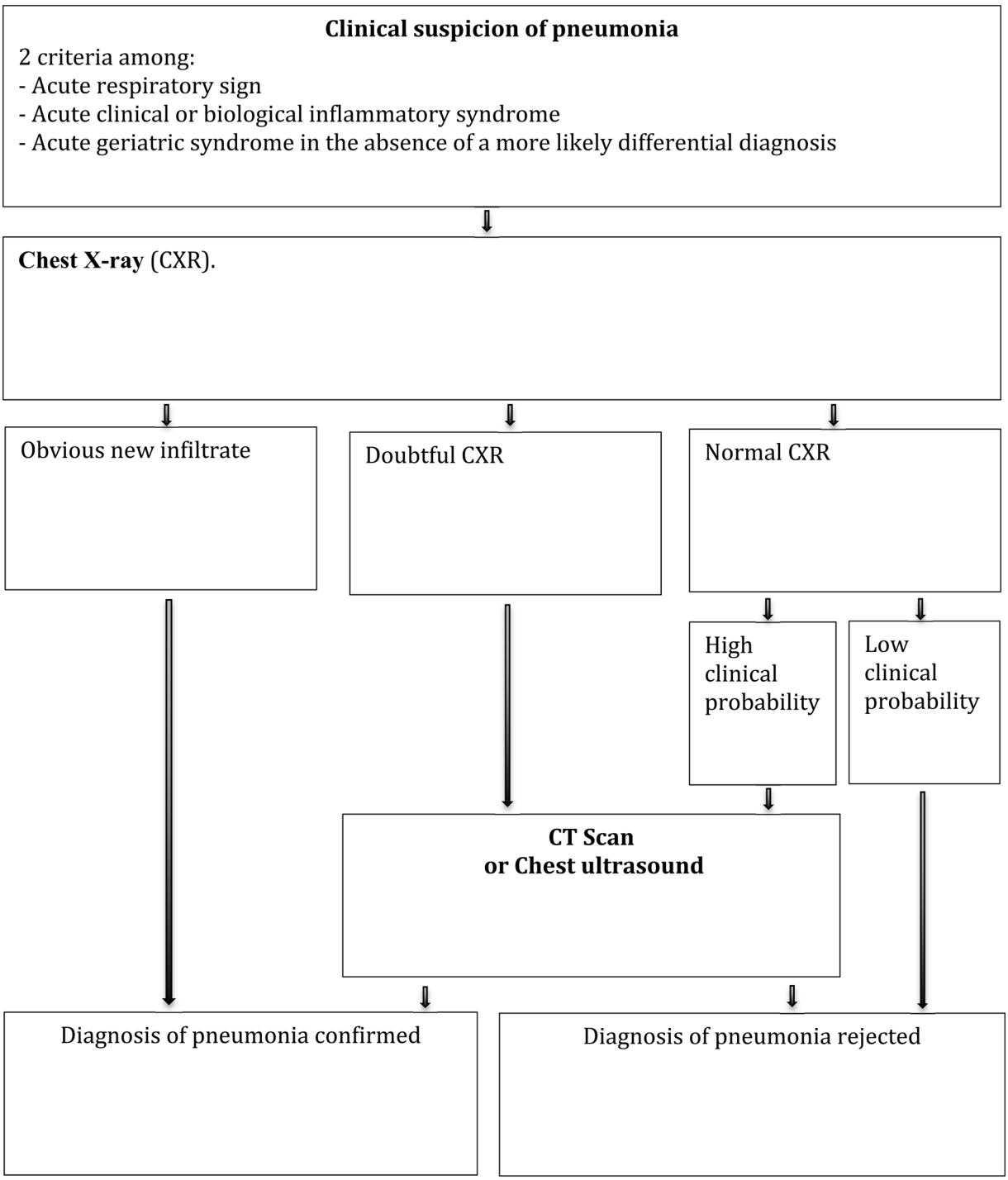
Clinical suspicion of pneumonia
2 criteria among:
- Acute respiratory sign
- Acute clinical or biological inflammatory syndrome
- Acute geriatric syndrome in the absence of a more likely differential diagnosis
Chest X-ray (CXR).
Obvious new infiltrate
Doubtful CXR
Normal CXR
High clinical probability
Low clinical probability
CT Scan or Chest ultrasound
Diagnosis of pneumonia confirmed
Diagnosis of pneumonia rejected

Fig. 3. Radiological diagnostic algorithm for pneumonia in older patients.

may be effective when performed by a suitably trained observer [29]. LUS was more sensitive than CXR (92 % vs 47 %) in an acute geriatric unit, with comparable specificity (94 % vs 93 %) [30]. POCT LUS helped discriminate pneumonia from other diagnoses (e.g. acute heart failure or pleural disease) in emergency and internal medicine wards. However, evidence is scarce in the geriatric setting [31]. The learning curve for LUS is steep, meaning that it can be easily taught to a large number of clinicians. [31] Whether improvement in diagnostic accuracy translates in a clinical benefit has still to be demonstrated. Another concern relates to the performance of LUS in a real-world setting when examinations are done by less expert teams.

The ongoing OCTOPLUS trial compares diagnostic, clinical and economic outcomes in older patients randomized to diagnostic strategies based on CXR, CT scan and POCT LUS [32].

3.3. *Biomarkers*

The added value of C reactive protein (CRP) or procalcitonin (PCT) to clinical signs and symptoms is low [33,34]. In a meta-analysis of patient-level data, adding CRP to clinical data improved the area under the receiver operating characteristic curve only by 0.075 [35]. Newly proposed biomarkers (e.g. neopterin, Serum amyloid A) are not better than CRP [27]. U.S. guidelines do not recommend the use of PCT for the diagnosis of CAP and stress that biomarkers should always be

interpreted in a clinical context [16]. Although CRP has an excellent negative predictive value in pneumonia [36], it may show a delayed increase during a bacterial infection, resulting in false-negative results in the early stages of the disease [37]. Moreover, some conditions are associated with artificially lower levels, such cirrhosis and hypoproteinaemia or immunosuppressive drugs [66] [67]. Another challenge seems to be the differentiation between inflammation and infection using CRP [68]. Among influenza, hospital mortality has been associated with a phenotype combining immunoparalysis with hyperinflammation which has been identified by determining ferritin and HLA-DR expression [38]. B-D-Glucan has been used for the diagnosis of *Pneumocystis jirovecii* pneumonia [20]. A further concern is the underrepresentation of older patients in most studies. Older patients may have higher baseline levels of inflammatory biomarkers due to chronic inflammation associated with comorbidities or the ageing process, hence lowering their accuracy to diagnose pneumonia [39].

3.4. Microbiological samples

Recommendations for microbiological samples collection vary according to the clinical context and severity of the disease. Even with extensive sampling, the pathogen is rarely identified, and identification will often not alter the antimicrobial treatment [40]. In patients hospitalised for pneumonia, it is proposed to obtain two pairs of blood cultures and good quality sputum samples before administration of antibiotics in patients able to expectorate. The latter is particularly recommended in patients with chronic respiratory disease. Collection of the samples should not delay the administration of antimicrobials. Urine antigen testing for *Legionella pneumophila* is recommended in evocative or severe cases. A urine antigen test for *Streptococcus pneumoniae* is recommended in severe [16,41,42] or, for some guidelines, moderately severe [41,42] CAP, as positivity may help narrowing the antibiotic spectrum.

If Methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected, a negative nasal swab for MRSA detection by PCR may allow to stop anti-MRSA therapy [43] .

Testing for SARS-CoV-2, and influenza should be considered in time of epidemics since the results will affect the treatment. Testing for other respiratory viruses frequently found in older patients such as RSV may allow antibiotics sparing and implementing prevention measures in nursing-homes and hospitals. Rhinovirus and metapneumovirus are frequent in inter-epidemic periods of influenza [44]. Bronchoalveolar lavage is rarely performed in older patients and is reserved for patients hospitalised in intensive care units or for whom probabilistic treatment has failed.

Testing for tuberculosis is justified in suggestive clinical or radiological presentations, including a subacute or chronic course, weight loss, haemoptysis, or cavitary infiltrates in developed countries and systematically in LMIC. Due to insufficient accuracy, tuberculin skin test and interferon-gamma-releasing assays have no place for the diagnosis of active tuberculosis [45].

3.5. Prognostic assessment

The severity of infection is assessed based on clinical evaluation and often comforted by the use of validated prognostic scores. The most used are the Pneumonia Severity Index (PSI), based on 20 demographic, clinical and biological characteristics [46], and CURB-65, a score that incorporates confusion, urea >7 mmol/L , respiratory rate >30 min, blood pressure <90 mmHg (systolic) or <60 mmHg (diastolic), and age ≥65 years [47]. Their performance in predicting mortality decreases with age, probably because they do not account sufficiently for comorbidities. [48,49]. SMART-COP score and ATS criteria may be used to predict the need for intensive or vasopressor support [16,50]. Many scores based on comorbidities, functional status, frailty, and sometimes combining laboratory data have been published, and need further validation [51–53].

Table 2
First-line probabilistic antibiotic regimens recommended by recent National guidelines for non-severe community acquired pneumonia in patient aged over 75, without allergy or risk factor for resistant pathogens.

Antibiotic regimen	Outpatient	Inpatient (outside ICU)
Monotherapy		
Penicillin G		Europe [41]
Amoxicillin	Australia [116], Europe, Great-Britain [42], Korea [117]	Europe
Amoxicillin-clavulanate / Ampicillin-sulbactam	China, France [118], Germany [119], Japan [120], Korea, South Africa [121]	Brasil [122], Europe, France, Germany, Japan, Korea, South-Africa
Doxycyclin	Australia, Europe	
Levofloxacin / Moxifloxacin	Europe, France, Korea, Spain [123], USA [16]	Brasil, Europe, France, Korea, Spain, USA
Oral Cephalosporins	China, Korea, South-Africa	South-Africa
IV Cephalosporins	France	Brasil, Europe, France, Germany, Korea, South Africa, Japan
Combination therapy		
Penicillin G -Macrolides		Australia, Europe
Amoxicillin-Macrolides	Brasil, Spain	Great Britain, Europe
Amoxicillin-Doxycyclin		Australia
Amoxicillin-clavulanate-Macrolides	Brasil, China, Korea, Spain, USA	Brasil, Europe, Germany, Spain, USA
Oral Cephalosporins-Macrolides	China, Korea, Spain, USA	
IV Cephalosporins-Macrolides		Brasil, Europe, Germany, Spain, USA

ICU: Intensive Care Unit.

4. Antibiotic treatment

The use of antibiotics in the management of pneumonia varies considerably from country to country. These variations stem from different thresholds to accept the risk of antibiotic therapy failure, and of the appreciation of the microbiological impact of antibiotic therapy at the individual and societal level. Accordingly, there are wide variations in national guidelines (table 2), which cannot be explained by microbiological variations alone. Current recommendations state that antibiotic treatment should be started as soon as the diagnosis is made. [41] However, the wish to treat early is in tension with the accuracy of the diagnosis, prompt treatment being associated with overdiagnosis, and if no sepsis, treatment can be deferred to complete the diagnostic path while continuing to monitor the patient [54]. Treatment effectiveness should be assessed after 72 h. The therapeutic strategy needs to account for the frequent diagnostic uncertainty; in the absence of severe disease, antibiotic therapy should be stopped as early as possible when the probability of pneumonia is low or when another diagnosis is more likely. Whenever possible, the oral route, which has shown equivalent efficacy with a lower iatrogenic risk, should be preferred [55,56]. The management of pneumonia in older patients has its own specific features, mainly due to the age-related changes in the upper airway's microbiota, as aspiration is the main pathophysiological pattern in this age group. Use of subcutaneous perfusion has an important role among elderly with therapeutic limitations [57]. We refer the readers to comprehensive recent reviews on challenges in optimization of antibiotics [57–59] to be applied among older adults. Internists should partner with geriatricians, infectious disease specialists, pneumologists and pharmacists to improve patients care [57,60].

4.1. Choice of empiric treatment

In most countries, the preferred probabilistic antibiotic treatment relies on beta-lactam drugs, frequently amoxicillin / clavulanate. In cases of true allergy, levofloxacin or moxifloxacin are the most recommended alternative. Fluoroquinolones are not recommended as a first-line treatment because of the rapid acquisition of bacterial resistance, the major impact in the selection of multidrug resistant pathogens, and adverse effects which, although rare, are potentially severe (torsade de pointes, tendon rupture, encephalopathy) [61,62]. The European Federation of Internal Medicine has published an adaptation of CAP guidelines to the internal medicine setting [63].

Table 2 presents recommendations issued by local societies in different countries. Whether combination antibiotic therapy should be preferred to monotherapy is still controversial [64]. Combination antibiotic therapy is recommended in several guidelines for moderately severe CAP (hospitalized in medical wards), [16] [42], though monotherapy with beta-lactams being non-inferior in terms of 3-month mortality in a large cluster-randomised trial [65]. However, a randomised trial failed to demonstrate the non-inferiority of monotherapy in patients hospitalised for pneumonia to reach clinical stability by day 7. Of note, non-inferiority was achieved once the most severe forms (PSI category 4 or more) or infections with atypical bacteria had been excluded [66].

In severe pneumonia, i.e. patients usually admitted to intensive care settings, combination antibiotic therapy is recommended in all guidelines. The rationale is to broaden the spectrum with an antibiotic covering intracellular pathogens (macrolides or fluoroquinolones) [26]. The immunomodulatory effect of macrolides could also be beneficial, which explains why macrolides are preferred over fluoroquinolones in the latest European recommendations [26]. However, macrolides and fluoroquinolones are associated with increased risk of cardiac arrhythmia [67], and macrolides have a potential for drug-drug interactions, which can be identified using adequate interaction checkers, and prevented, adjusting multiple drug regimens [57].

Of note, antibiotic resistance is lower in Northern Europe than Western Europe, where countries such as Italy and Greece are flagellated with multidrug resistant pathogens.

4.2. Anaerobic coverage

A questionable common practice is to cover anaerobes extensively, by adding metronidazole or clindamycin to the recommended antibiotic therapy. While it has been thought that anaerobic bacteria were frequent in pneumonia in the very old, particularly in AsP, recent microbiological data have reopened the debate [17,68], and previous post-mortem studies may have largely overestimated anaerobic involvement. Moreover, beta-lactam antibiotics in general, and the combination of amoxicillin and clavulanate in particular, have good activity against most anaerobic bacteria. Hence, adding metronidazole is not rational for supra-diaphragmatic infections, with the exception of abscesses. Recent guidelines propose no specific anti-anaerobic therapy for AsP [16]. Antibiotics targeting anaerobes may actually be harmful through their major impact on gut microbiome, depletion of anaerobic bacteria being associated with an increase in bacterial pneumonia, lung injury and mortality [68].

4.3. Duration

The duration of antibiotic treatment for pneumonia should not exceed five days if the course is favourable, whatever the age [69]. There are no data to support prolonged treatment in AsP or frailty. Inflammatory markers, especially PCT, could be useful to safely reduce the duration of antibiotic treatment [70].

4.4. Treatment failure

Apart from specific situations (multiple hospitalisations, chronic lung disease, bronchiectasis), antibiotic resistance to respiratory pathogens remains low, at least in Northern Europe, and non-sensitivity to the antibiotics administered is less frequent than diagnostic error. However, this is in contrast with other European countries where prevalence of antimicrobial resistance is very high. Hence optimizing antibiotic therapy is a global public health emergency [71]. When the evolution is unsatisfactory, a meticulous search for another diagnosis or complications should be preferred to “blind” antibiotic escalation. A chest CT scan may confirm the diagnosis and identify complications (empyema, abscess) or propose differential diagnoses (e.g. pulmonary embolism, heart failure, lung cancer). Diffuse lung disease (cryptogenic organising pneumonia, lung fibrosis, granulomatous disease) or unusual pathogens (mycobacteria, nocardia, pneumocystis) can also be suggested by the pattern and distribution of lung involvement on CT-scan.

5. Non-antibiotic treatment

5.1. Corticosteroids

Corticosteroids as adjuvant treatment in pneumonia reduce the risk of treatment failure, length of hospital stay, and time to clinical stability [72]. The impact on mortality is less obvious, the two more recent large clinical trials in severe CAP having conflicting results. A U.S. study included 586 patients admitted to the ICU and randomized to 40 mg methylprednisolone or placebo daily. There was no significant difference in 60-day mortality (16 % vs. 18 %, $p = 0.61$) [73]. In contrast, a French study randomized 800 patients admitted to the ICU to 200 mg hydrocortisone or placebo daily. The 28-day mortality was halved, and generally lower (6.3 % vs. 11.9 %, $P = 0.006$) [74]. The most plausible explanation for these conflicting results is the delay in starting treatment. The French trial administered steroids within 24 h of eligibility (median: 15 h) whereas the US trial allowed inclusion up to 96 h (median: 37 h). These results favour early initiation of hydrocortisone in adult patients with severe CAP. Unfortunately, the therapeutic effects of corticosteroids are often accompanied by clinically significant side effects, most of which are related to the dose and duration of therapy [75]. In existing literature, the duration of corticosteroid treatment is most frequently 7–10 days, however shorter duration (e.g. 4 days) appears to be effective in improving evolution [75], although the only published trial with a single dose of corticosteroid was negative [76]. Most adult trials used steroid doses equivalent to 40 mg to 50 mg of prednisone per day. The current U.S. guidelines [45] have not endorsed the routine use of corticosteroids for patients with severe CAP, while the European guidelines recommend their use only for severe CAP with concurrent shock [77]. Differentiating the phenotypes of responders and non-responders is a research priority [78,79]. The administration of corticosteroids must take into account the risk of gastric bleeding in these patients who also should receive anti-thrombotic prophylaxis (or treatment). The addition of proton pomp inhibitor therapy at the acute phase of pneumonia seems reasonable in patients at risk of gastric bleeding (peptic ulcer disease, anti-thrombotic treatment) [80,81].

Conversely, there is no convincing evidence for large scale use of corticosteroids in non-severe pneumonia (i.e. outside intensive care units), because the small decrease in length of stay might be compensated by adverse events when corticosteroids are administered in a non-selected population with a high proportion of false diagnosis. Furthermore, in a recent meta-analysis of existing trials, corticosteroids in CAP were associated with a greater benefit in younger patients; the mortality benefit being not significant after 70 years [82].

5.2. Aspiration management

Aspiration is the main source of pneumonia in the very old.

Dysphagia, prior episodes of coughing on liquid (or food) intake, or gravity-dependent shadow distribution in Chest X rays are key points to suspect aspiration [83]. The management of AsP is complex and prognosis depends at least as much on treatment of the cause as on antibiotic therapy, since AsP frequently recurs despite microbiological success. Usual probabilistic treatment is recommended and there is no rational to broaden antibiotic spectrum nor extend treatment duration in recurrence. Indeed, escalation of antibiotic treatment may affect the microbiota, select for microbiological resistance and thus compromise the success of future antibiotic therapy.

Aspiration prevention is paramount, requires comprehensive care, and should be conducted concurrently with antibiotic treatment. Installing patients in a seated, or at least semi-recumbent position is warranted, as patients in the supine position are prone to silent aspiration and early recurrence [83]. Prevention of recurrence also involves swallowing rehabilitation, meticulous oral care, meal and textures adaptation. Respiratory and general rehabilitation, active mobilization to prevent bed lying, avoidance of selected drugs (psychotropic drugs, proton pump inhibitors), and early re-nutrition are also important. [84]

While macro-aspiration results in chemical pneumonitis, it does not necessarily cause bacterial pneumonia and does not require systematic antibiotic treatment, as the acidic gastric fluid is usually sterile. Following an aspiration event, an expectant attitude, aiming to begin antibiotics only if deterioration of respiratory function or fever develops in the next 48 h should be preferred [85].

5.3. Prevention

In addition to managing the very common predisposing pathologies (Parkinson's or cerebro-vascular disease, heart failure…), measures to prevent the onset of pneumonia in the elderly are needed including stopping or reducing tobacco and alcohol consumption, improving oral and dental hygiene, physical exercise, avoiding contact with people suffering from respiratory infections combating undernutrition and iatrogenicity (proton pump inhibitors, neuroleptics, benzodiazepines, immunosuppressants), and vaccinations against pneumococcus, influenza, SARS-CoV-2, RSV [86] and soon metapneumovirus [87]. However pneumonia may sometimes not be preventable because of advanced ages and high comorbidity burden [88].

5.4. Oral care

Micro- or-macro- aspiration of oropharyngeal contents being the main source of bacterial infection of the lungs in the elderly, decreasing the concentration of pathogenic bacteria in the mouth is a logical prevention measure. This preventive strategy has recently proved highly effective to prevent ventilator-associated pneumonia [89]. Indeed, active aid in teeth brushing decreases incidence of pneumonia and pneumonia-related mortality in nursing-home residents [90]. However, intensive treatment and involvement of specialized dental personnel might be required to reach this benefit [91] .

5.5. Nutritional support

The choice of the route of feeding is a key question after AsP. This complex decision involves both prognostic and ethical considerations, and requires a multidisciplinary approach respecting patient's wishes. Patients ingesting <60 % of the recommended daily allowance for more than one week have a worse prognosis [92]. There is considerable heterogeneity in practice regarding the use of enteral and parenteral nutrition (table 4). However, recent data demonstrate the importance of adequate nutritional intake, whatever the route, on short-term prognosis. A secondary analysis of a trial analysed patients with lower respiratory tract infection, randomised to receive individualised nutritional support (intervention group) or standard hospital diet (control group). Although the difference did not reach significance, mortality was halved in the intervention group [93]. In a large observational study of very old Japanese patients with AsP, increased parenteral calories and amino acid doses were associated with reduced in-hospital mortality [94].

5.6. Pneumonia at the end of life

Pneumonia is a frequent terminal event in old and multimorbid patients, and there is no consensus on how to diagnose and treat it. Whether antibiotics should be prescribed to try to prolong survival or lessen patients symptoms remains controversial [95]. In this situation, palliative care should be promptly provided, and prescription of antibiotics used in a rational manner to limit antibiotic resistance [96]. Other medications (antipyretics, antalgic drugs, anti-cholinergic drugs) and measures (stopping fluid administration) may be more indicated in terms of medical ethics [97].

5.7. Prevention of early complications

The geriatrician's added value in the care of pneumonia lies mainly in the early detection and management of co-morbidities. A comprehensive geriatric assessment includes addressing malnutrition, iatrogenesis, motor, nutritional, cognitive, psychological and social frailties. A particular attention should be paid to the detection, prevention and management of delirium, which is common in the course of pneumonia and is strongly associated with poor outcomes [98]. The presence of delirium during the acute phase of the infection should not prevent from motor rehabilitation and geriatric rehabilitation, as delirium does not influence the recovery trajectory of ADL functioning and quality of life [99].

5.8. Cardiovascular complications

The link between pneumonia and cardiovascular events is increasingly documented, for myocardial infarction [100], stroke [101], acute heart failure [102] and thromboembolism [103]. One-third-of patients hospitalised for pneumonia will present a cardiovascular complication [104], the occurrence of which increases in-hospital mortality fivefold [105]. Thromboprophylaxis is recommended for hospitalised patients during the acute phase [106]. The value of antiplatelets drugs for the prevention of arterial events after pneumonia is suggested in observational [102,107] and interventional studies [108] and is currently being evaluated in on-going trials [109]. Older patients are particularly at risk for type 2 myocardial infarction, i.e. myocardial ischaemia without atherothrombotic events, secondary to an imbalance between myocardial oxygen supply and enhanced demand [110]. These functional myocardial infarctions are often painless and require close clinical monitoring. Although the cardiovascular risk persists for months after pneumonia [102] with a significantly higher risk of cardiovascular event (myocardial infarction, stroke) during two years [104], the vast majority of cardiac events occur on the first day following the diagnosis of pneumonia [111].

5.9. Functional decline

Functional decline following pneumonia is often severe, particularly in frail older adults. Sixty percent of older patients hospitalised for pneumonia will experience a deterioration in functional status. Frailty is a better predictor of functional trajectory than the severity of pneumonia itself, and preventive policies of early physiotherapy particularly benefit moderately frail or pre-fragile patients [112].

In a longitudinal study evaluating cognitive trajectories five years after hospitalisation for pneumonia, a transient cognitive decline was found when compared with a matched control population [113]. However, it remains uncertain whether pneumonia itself or the iatrogenic effect of hospitalisation are responsible. A long-term impact of the infectious episode on neurocognitive impairment is debated [113,114].

Table 3
Common mistakes in antibiotic management of acute pneumonia in older patients.

Common mistake	Alternative	Rational
Antibiotic treatment for >7 days	-Antibiotic treatment for 5 days if favourable evolution whatever age and frailty -CRP and PCT-guided treatment algorithms may help reducing the duration of antibiotic therapy	- Proven non-inferiority of short duration - Less impact on the microbiota
Addition of a specific anaerobic agent (metronidazole or clindamycin) for aspiration pneumonia (excluding pulmonary abscesses).	- Amoxicillin-clavulanate (or piperacillin-tazobactam if late nosocomial infection >5 days of hospital stay)	- Low involvement of anaerobes in non-abscessed pneumonia - Sensitivity of oral anaerobes to amoxicillin/clavulanic acid - Major impact on the gut microbiota
Therapeutic escalation in the case of positive respiratory samples taken under antibiotic treatment	Sample taken before any antibiotic treatment or in the event of microbiological failure only	- Respiratory samples taken while on antibiotics reflect the surviving flora of the upper airways but not necessarily the pathogen.
Therapeutic escalation due to aspiration recurrence	-Treatment of the cause (s) of aspiration -Short course of narrow-spectrum antibiotics	- This is a recurrence, not a microbiological failure. - Any escalation of treatment selects for resistance and affects the microbiota.
Therapeutic escalation due to rising CRP at 48–72h	-Clinical assessment of progress -Use of rapid kinetic parameters (leucocytes, procalcitonin)	- Slow kinetics of CRP with a peak delayed by 3 days

The incidence of post-pneumonia neurovascular events could explain an increased risk of neurocognitive disorders of vascular origin [114].

The nutritional decline associated with pneumonia, due to hypercatabolism and intake deficiency, is often major and requires specific management. Nutritional parameters are highly predictive of post-pneumonia survival [115]. Appropriate early nutritional management, considering the risk associated with aspiration but also with the re-nutrition process (table 4), may limit sarcopenia induced by the infection.

6. Conclusion

Pneumonia remains the leading cause of infection-related death in older patients. Collaboration between geriatricians, internists and infectious disease physicians is paramount. The atypical presentation and simultaneous presence of comorbidities often compromise the accuracy of physical and radiological findings. To avoid both under and over diagnosis, the use of CT or lung ultrasound is recommended in uncertain cases. Aspiration is the predominant mechanism of pneumonia in frail older patients and *Enterobacteriaceae* coverage should be considered. However, extended anti-anaerobic coverage is not required. A 5-days treatment is frequently effective and limits the impact on microbiome. Early care is multidimensional and should involve consideration for cardiovascular involvement, prevention of delirium, and nutritional assessment and support. Given the heavy functional burden of pneumonia, early respiratory and motor rehabilitation are needed. As pneumonia is a frequent event at the end of life, palliative care should not be delayed.

Table 3

Table 4
Nutrition alternatives in patients with aspiration pneumonia.

Nutrition mode	Advantages	Disadvantages	Preferred indications
Fasting	Lower risk of aspiration	Malnutrition	- Palliative care Or - Acute phase <72h
Oral diet +/- oral nutritional supplement	Eating pleasure	High risk of aspiration	- Palliative care Or - Satisfactory nutritional status and oral intake >60 % of recommended daily allowance
Enteral by nasogastric tube	Effective renutrition Prevention of villous atrophy	Risk of aspiration Discomfort Frequent accidental removal if delirium	- Nutritional support < 1 month And - 30–45° supine position possible
Enteral by gastrostomy	Effective renutrition Prevention of villous atrophy	Invasive procedure (percutaneous or endoscopic)	- Nutritional support >1 month And - -Low aspiration risk
Enteral by jejunostomy	Effective renutrition Prevention of villous atrophy Lower risk of aspiration than other oral / enteral feeding methods	Surgical procedure	- Nutritional support >1 month And - High aspiration risk
Parenteral	Lower risk of aspiration	Frequent need of a central venous catheter Iatrogenic risk (metabolic disorders, catheter infection, volume overload) Accidental removal if delirium Lower quality of renutrition than enteral feeding	Acute reversible cause of non-functional digestive tract.

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Ethical disclosure

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